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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/294,494	04/20/99	EDELSON	R 270425.003

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ATTN: ANITA LOMARTRA

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EXAMINER	
NGUYEN, Q	
ART UNIT	PAPER NUMBER
1632	10

DATE MAILED: 11/07/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/294,494	EDELSON, RICHARD LESLIE	
	Examiner	Art Unit	
	Quang Nguyen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 August 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-27,46-60,64 and 65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-27,46-60,64 and 65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendment filed August 14, 2001 in Paper No. 9 has been entered.

Claims 13-27, 46-60 and 64-65 are pending in the present application, and they are examined on the merits herein.

The text of those sections of Title 35 U.S.C. Code not included in this action can be found in a prior office action.

Claim Rejections - 35 USC § 102

Claims 13-21 and new claim 64 are rejected under 35 U.S.C. 102(a) as being anticipated by Garbe et al. (Blood 92, No. 10, Supplement 1, 165a, 1998, PTO-1449 in paper no. 4) as set forth in the previous Office Action in Paper No. 7.

The claims are drawn to a composition comprising functional dendritic antigen presenting cells derived from monocytes which have been incubated following their treatment by at least one of: (1) exposure to physical perturbation, (2) irradiation in the presence of a photoactivatable agent that forms photoadducts with cellular components, or (3) treatment with a DNA binding agent; the same composition further comprising at least one of GM-CSF or IL-4 (claim 20) or the same composition wherein it further comprises at least one selected antigen for presentation by the dendritic cells (claim 21).

Garbe et al. disclose the generation of CD1a+ dendritic cells from adherent cultured peripheral monocytes in the presence of IL-4, GM-CSF and TGFβ under

serum-free conditions within 5 days of culture (second full paragraph, lines 6-9). Garbe et al. further teach that in the presence of both TGFβ and tetanus toxoid, the generated dendritic cells were less effective to stimulate the proliferation of primed autologous T-cells as compared to dendritic cells being depleted of TGFβ before being matured in the presence of TNF-α (second paragraph, lines 12-16). It is noted that the instant claims are composition by process claims, and the composition comprising CD1a+ dendritic cells disclosed by Garbe et al. is indistinguishable from that of the present invention. For this instance, the processes in making the same composition are not given any patentable weight. Furthermore, there is no disclosure of a feature to the claimed composition that distinguishes it from the composition of Garbe et al. Therefore, Garbe et al. anticipate the instant claimed invention.

Responses to Arguments

Applicants' arguments related to the above rejection in the Amendment filed on August 14, 2001 in Paper No. 9 (pages 8-9) have been fully considered.

Applicants mainly argued that "Garbe et al. does not teach or suggest a composition in which dendritic cells are formed in a short time and in which the age of the dendritic cells in the composition is relative uniform". Applicants further argued that the cell culturing process of Garbe et al. takes five days instead of 6 to 48 hours in the process of the instant invention, therefore the age of the dendritic cells generated in the process of Garbe et al. varies widely and a composition comprising such dendritic cells is not effective in presenting antigens as the composition containing dendritic cells of

the presently claimed invention. Examiner respectfully finds Applicants' arguments to be unpersuasive for the following reasons.

Firstly, the instant claimed composition is not limited to a composition comprising functional dendritic antigen presenting cells of relatively uniform age, at any particular stage of dendritic cell differentiation. Secondly, there is no factual evidence indicating that the functional dendritic antigen presenting cells in the claimed composition possess any distinct cell markers to distinguish themselves from those in the composition taught by Garbe et al. Thirdly, there is also no factual evidence indicating that the dendritic cells in the composition disclosed by Garbe et al. are not as effective in presenting antigens as those of the instant claimed composition. Furthermore, MPEP 2112.01 clearly states that "If the composition is physically the same, it must have the same properties".

Accordingly, claims 13-21 and 64 remain rejected for the reasons set forth above.

Claims 13-21 and new claim 64 are rejected under 35 U.S.C. 102(e) as being anticipated by Tedder et al. (U.S. Patent No. 5,849,589) as set forth in the previous Office Action in Paper No. 7.

Tedder et al. disclose a composition comprising induced differentiated monocytes into dendritic cells in the presence of GM-CSF, IL-4 and TNFα (column 2, lines 19-37). The monocytes are plastic adherent human blood monocytes (col. 2, lines 48-49). Furthermore, Tedder et al. teach that the dendritic cells are plated in cultured

dishes and exposed to antigen in a sufficient amount and for a sufficient period of time to allow the antigen to bind to the dendritic cells (column 11, lines 51-57).

As noted above the instant claims are composition by process claims, and there is no disclosure of a feature to the claimed composition that distinguishes it from the composition of Tedder et al. Therefore, Tedder et al. anticipate the instant claimed invention.

Responses to Arguments

Applicants' arguments related to the above rejection in the Amendment filed on August 14, 2001 in Paper No. 9 (page 9) have been fully considered.

Applicants mainly argued that "Tedder does not teach or suggest a composition containing dendritic cells in which the age of dendritic cells is relatively uniform". Examiner respectfully finds Applicants' arguments to be unpersuasive for the same reasons stated above. Basically, the instant claimed composition is not limited to a composition comprising functional dendritic antigen presenting cells of relatively uniform age, at any particular stage of dendritic cell differentiation. There is no factual evidence indicating that the functional dendritic antigen presenting cells in the claimed composition possess any distinct cell markers to distinguish themselves from those in the composition taught by Tedder. Nor is there any factual evidence indicating that the dendritic cells in the composition disclosed by Tedder are not as effective in presenting antigens as those of the instant claimed composition. Furthermore, MPEP 2112.01

clearly states that "If the composition is physically the same, it must have the same properties".

Accordingly, claims 13-21 and 64 remain rejected for the reasons set forth above.

Claims 13-21 and new claim 64 are rejected under 35 U.S.C. 102(e) as being anticipated by Edelson et al. (U.S. Patent No. 5,820,872, PTO-1449 in paper no. 2) as set forth in the previous Office Action in Paper No. 7.

Edelson et al. disclose a preparation comprising a leukocyte preparation, including monocytes, being exposed to irradiation in the presence of a photoactivatable agent to form a photo-inactivated cell preparation which is further exposed to a plurality of tumor-derived antigens to form cellular vaccine (column 4, lines 40-48; column 5, lines 8-31; column 11, lines 22-59). In addition, Edelson et al. teach that for enhancing expression of empty major histocompatibility complex molecules, the cell preparation is further contacted with a cytokine including granulocyte monocyte conlony stimulating factor (column 9, line 66 continues to line 12 of column 10).

As noted previously the instant claims are composition by process claims, and there is no disclosure of a feature to the claimed composition that distinguishes it from the composition of Edelson et al. Therefore, Edelson et al. anticipate the instant claimed invention.

Responses to Arguments

Applicants' arguments related to the above rejection in the Amendment filed on August 14, 2001 in Paper No. 9 (pages 9-10) have been fully considered.

Applicants argued that "the Edelson '872 does not teach or suggest a method for producing dendritic cells". Additionally, Applicants argued that "the method described by Edelson '872 patent does not involve the induction of dendritic cells at all, but merely the induction of empty class I MHC molecules at the surface of antigen presenting cells already present in the subject's blood". Examiner respectfully finds Applicants' arguments to be unpersuasive because the Edelson '872 patent clearly teach a composition comprising a leukocyte preparation, preferably monocytes, exposed to one of the following conditions: (1) photospheresis, (2) temperatures less than physiological temperatures and (3) contacting the cellular preparation with one or more cytokines, to induce expression of major histocompatibility molecules (col. 4, line 51 continues to line 31 in col. 5). Moreover, the Edelson '872 patent teaches that the monocytes being exposed to irradiation in the presence of a photoactivatable agent to form a photo-inactivated cell preparation which is further exposed to a plurality of tumor-derived antigens to form cellular vaccine (column 4, lines 40-48; column 5, lines 8-31; column 11, lines 22-59). In subjecting the monocytes under photospheresis conditions disclosed by the Edelson '872 patent, the dendritic cells would be certainly generated and present in the composition disclosed by the Edelson '872 patent, because the same photospheresis conditions are utilized in the instant claimed invention. Furthermore, MPEP 2112.02 clearly states that "While the references do not show a specific

recognition of that result, its discovery by appellants (the induction of differentiation of monocytes into functional dendritic antigen presenting cells under photospheresis condition) is tantamount only finding a property in the old composition".

Accordingly, claims 13-21 and 64 remain rejected for the same reasons set forth above.

Claims 13-20 and new claim 64 are rejected under 35 U.S.C. 102(b) as being anticipated by Akagawa et al. (Blood 88:4029-4039, 1996) as set forth in the previous Office Action in Paper No. 7.

Akagawa et al. disclose the generation of CD1+relB+ dendritic cells from adherent human monocytes in the presence of GM-CSF plus IL-4. The monocyte-derived dendritic cells can be maintained in the terminally differentiation of dendritic cells with TNFα (See abstract and page 4032, column 2, second and third full paragraphs). Since there is no disclosure of a feature to the claimed composition that distinguishes it from the composition of Akagawa et al., the reference anticipates the claimed invention.

Responses to Arguments

Applicants' arguments related to the above rejection in the Amendment filed on August 14, 2001 in Paper No. 9 (pages 10-11) have been fully considered.

Applicants mainly argued that Akagawa does not teach or suggest a composition containing an optimum number of functional antigen presenting dendritic cells as the

composition of the presently claimed invention. Examiner respectfully finds Applicants' arguments to be unpersuasive for the same reasons stated in the responses related to the cited references of Garbe et al. and Tedder et al. above.

Claims 13-23 and new claim 64 are rejected under 35 U.S.C. 102(e) as being anticipated by Cohen et al. (U.S. Patent No. 6,010,905) as set forth in the previous Office Action in Paper No. 7.

The claims are drawn to a composition comprising functional dendritic antigen presenting cells derived from monocytes which have been incubated following their treatment by at least one of: (1) exposure to physical perturbation, (2) irradiation in the presence of a photoactivatable agent that forms photoadducts with cellular components, or (3) treatment with a DNA binding agent.

Cohen et al. teach a preparation of monocytes having increasing the antigen presenting ability including those with the phenotype of an activated myeloid dendritic cell by contacting the monocytes with an agent, preferably a calcium ionophore, which elevates the intracellular calcium concentration to a level sufficient and effective to increase said antigen presenting ability (column 4, lines 13-18, column 5, lines 5-12). Cohen et al. disclose that the same composition further treated with a second agent selected from the group consisting of rhGM-CSF, rhIL-4, rhIL-12, rhIL-2, and rhTNFalpha (column 5, lines 5-12). Cohen et al. also teach contacting the monocytes isolated from the blood of a subject with a cancer with an agent which increases the intracellular calcium concentration, thereby enhancing the antigen presenting ability of

the monocytes, then exposing the monocytes to tumor antigens from the cancer. The treated monocytes cells are then transferred back into the patient with the cancer for treatment purposes (column 5, lines 34-43). Cohen et al. also teach that the dendritic cells can also be challenged with antigens from the surface of HIV-1 or other disease carrying agents such as cancer cells of the breast, brain, liver or stomach (column 38, lines 14-25).

As noted previously the instant claims are composition by process claims, and there is no disclosure of a feature to the claimed composition that distinguishes it from the composition of Cohen et al. Therefore, Cohen et al. anticipate the instant claimed invention.

Responses to Arguments

Applicants' arguments related to the above rejection in the Amendment filed on August 14, 2001 in Paper No. 9 (pages 11) have been fully considered.

Applicants mainly argued that the composition described in Cohen contains monocytes whose antigen presenting ability is enhanced, and that the composition is not comprised of functional antigen presenting dendritic cells induced from monocytes. Examiner respectfully finds Applicants' arguments to be unpersuasive because Cohen et al. clearly teach the preparation of monocytes having increasing the antigen presenting ability and with the phenotype of an activated myeloid dendritic cell by contacting the monocytes with an agent, preferably a calcium ionophore, which elevates the intracellular calcium concentration to a level sufficient and effective to increase said

antigen presenting ability and in the presence of a second agent selected from the group consisting of rhGM-CSF, rhIL-4, rhIL-12, rhIL-2, and rhTNAalpha (column 4, lines 13-18, column 5, lines 5-12). There is no factual evidence of record indicating or suggesting that the activated monocytes with the phenotype of an activated myeloid dendritic cell are functionally distinct structurally or functionally compared to the functional dendritic antigen presenting cells containing in the composition of the presently claimed invention.

Accordingly, claims 13-23 and 64 remain rejected for the same reasons set forth above.

Claim Rejections - 35 USC § 103

Claims 24-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Cohen et al. (U.S. Patent No. 6,010,905) or Garbe et al. (Blood 92, No. 10, Supplement 1, 165a, 1998, PTO-1449 in paper no. 4) or Tedder et al. (U.S. Patent No. 5,849,589) in view of Patel (U.S. Patent No. 5,167,657) as set forth in the previous Office Action in Paper No. 7.

Claims 24-27 are directed to a packaged preparation comprising: a composition comprising functional dendritic antigen presenting cells derived from monocytes which have been incubated following their treatment by at least one of: (1) exposure to physical perturbation, (2) irradiation in the presence of a photoactivatable agent that forms photoadducts with cellular components, or (3) treatment with a DNA binding

agent; and a container which does not leach plasticizer and which is sufficiently porous to permit exchange of gases for storing the composition.

Cohen et al. teach a preparation of monocytes having increasing the antigen presenting ability including those with the phenotype of an activated myeloid dendritic cell by contacting the monocytes with an agent, preferably a calcium ionophore, which elevates the intracellular calcium concentration to a level sufficient and effective to increase said antigen presenting ability (column 4, lines 13-18, column 5, lines 5-12). Cohen et al. disclose that the same composition further treated with a second agent selected from the group consisting of rhGM-CSF, rhIL-4, rhIL-12, rhIL-2, and rhTNFalpha (column 5, lines 5-12). Cohen et al. further teach contacting the monocytes isolated from the blood of a subject with a cancer with an agent which increases the intracellular calcium concentration, thereby enhancing the antigen presenting ability of the monocytes, then exposing the monocytes to tumor antigens from the cancer. The treated monocytes cells are then transferred back into the patient with the cancer for treatment purposes (column 5, lines 34-43). Cohen et al. also teach that the dendritic cells can be challenged with antigens from the surface of HIV-1 or other disease carrying agents such as cancer cells of the breast, brain, liver or stomach (column 38, lines 14-25). Garbe et al. disclose the generation of CD1a+ dendritic cells from monocytes in the presence of IL-4, GM-CSF and TGFβ under serum-free conditions within 5 days of culture (second full paragraph, lines 6-9). Garbe et al. further teach that in the presence of both TGFβ and tetanus toxoid, the generated dendritic cells were less effective to stimulate the proliferation of primed autologous T-cells as compared to

dendritic cells being depleted of TGFβ before being matured in the presence of TNF-α (second paragraph, lines 12-16). Tedder et al. disclose a composition comprising induced differentiated monocytes into dendritic cells in the presence of GM-CSF, IL-4 and TNFα (column 2, lines 19-37). Furthermore, Tedder et al. teach that the dendritic cells are plated in cultured dishes and exposed to antigen in a sufficient amount and for a sufficient period of time to allow the antigen to bind to the dendritic cells (column 11, lines 51-57). The compositions disclosed by Cohen et al., Garbe et al. and Tedder et al. are indistinguishable from those of the instantly claimed invention. However, Cohen et al., Garbe et al. and Tedder et al. did not teach the packaging of the disclosed compositions in a container which does not leach the plasticizer and which is sufficient porous to permit exchange of gases for storing the composition.

Patel discloses the making and using of flexible, autoclavable, plastic containers for storing red blood cells and these containers are able to suppress hemolysis of the red blood cells (See Summary of the Invention, columns 2 and 3).

Accordingly, at the time of the instant invention it would have been obvious to the ordinary skilled artisan to package the compositions disclosed by Cohen et al., Garbe et al. and Tedder et al. in the plastic containers taught by Patel for storage and for later use of the activated dendritic cells to treat patients in need of. Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

It is further noted that the rejection of the above claims can also be applied using the teachings of Edelson et al. (U.S. Patent No. 5,820,872, PTO-1449 in paper no. 2) or

Akagawa et al. (Blood 88:4029-4039, 1996) in view of Patel (U.S. Patent No. 5,167,657).

Responses to Arguments

Applicants' arguments related to the above rejection in the Amendment filed on August 14, 2001 in Paper No. 9 (pages 11-12) have been fully considered.

Applicants mainly argued that the Patel reference does not add anything to the teachings of Garbe, Tedder, Edelson, Akigawa or Cohen regarding to the compositions that are contained in the packaged preparations of the instant claims. Although Examiner agrees with Applicants on this point, Applicants' arguments regarding to the teachings of Garbe, Tedder, Edelson, Akigawa or Cohen are not found to be persuasive for the reasons already discussed above. Therefore, the packaged preparation of the instant claimed invention as a whole would have been obvious to one of ordinary skilled in the art in light of the combined teachings of either Garbe, Tedder, Edelson, Akigawa or Cohen in view of Patel.

Claims 13-27, 46-60 and new claims 64-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Edelson (WO 97/34472, PTO-1449 in paper no. 2) in view of any one of Tedder et al. (U.S. Patent No. 5,849,589) or Cohen et al. (U.S. Patent No. 6,010,905) or Garbe et al. (Blood 92, No. 10, Supplement 1, 165a, 1998, PTO-1449 in paper no. 4) and Patel (U.S. Patent No. 5,167,657) as set forth in the previous Office Action in Paper No. 7.

Claims 13-23 and 64 are drawn to a composition comprising functional dendritic antigen presenting cells derived from monocytes which have been incubated following their treatment by at least one of: (1) exposure to physical perturbation, (2) irradiation in the presence of a photoactivatable agent that forms photoadducts with cellular components, or (3) treatment with a DNA binding agent. Claims 46-59 and 65 are directed to a composition of co-incubated populations comprising: a first population including disease effector agents which express at least one disease associated antigen; and a second population including functional dendritic antigen presenting cells derived from monocytes which have been treated by at least one of: (1) exposure to physical perturbation, (2) irradiation in the presence of a photoactivatable agent that forms photoadducts with cellular components, or (3) treatment with a DNA binding agent; the same composition wherein the disease effector agents are selected from the group consisting of T-cell, B-cells and macrophages, and wherein the T cells include lymphoma cells, preferably cutaneous T-cell lymphoma cells; and wherein the composition further comprises at least one immunomodulatory agent. Claims 24-27 and 60 are drawn to packaged preparations comprising the above compositions in a container which does not leach plasticizer and which is sufficiently porous to permit exchange of gases for storing the composition.

Edelson teach that cultured dendritic cells can be added to or incubated with extracorporeal blood containing disease effector cells that has been treated via known photophoretic methods to increase the degree of immune responses for treating various diseases such as leukemia, lymphoma, autoimmune disease, graft versus host disease,

and transplanted tissue rejection (page 4, lines 20-28 and page 5, lines 8-12). The disease effector cells include and not limit to T cells, encompassing cutaneous T cell lymphoma, B cells, and/or infected white blood cells, such as virally or bacterially infected cells (page 5, lines 8-12 and page 2, line 4-11). Edelson further teaches that the agents that are used to treat disease effector cells include photoactivatable chemical agents such as psoralens (8-MOP), porphyrin, pyrenes, phthalocyanine; chemotherapeutic agents such as cyclophosphamide, methotrexate, cytokines including TNFalpha and interferon gamma; non-chemical agents such as UVA irradiation, X-ray irradiation, gamma-ray irradiation, and agents such as mitomycin C, cis-platinum among others (See pages 11-13 under section V). Edelson also discloses that the dendritic cells can be added or incubated with extracorporeal blood containing disease effector cells at any stage of the conventional phopheresis procedure (page 17, lines 5-11). It is also recognized that photophoresis induces the release and transfer of disease associated peptides from the treated disease effector cells to the MHC sites of the dendritic cells (page 16, lines 11-15, lines 20-23; page 22, lines 12-16). Moreover, Edelson discloses that such compositions are contained in a blood collecting bag (page 15, lines 19-28). However, Edelson does not specifically teach that functional dendritic cells in the disclosed compositions are derived from monocytes, or the time period required for the coincubation of the two cell populations to facilitate necessary direct cell to cell contact between the added dendritic cells and the treated disease effector cells or a container with recited properties.

Tedder et al. teach that monocytes can be induced to differentiate into functional dendritic cells in the presence of GM-CSF, IL-4 and TNFα in culture (column 2, lines 19-37). Furthermore, Tedder et al. teach that the dendritic cells are plated in cultured dishes and exposed to antigen in a sufficient amount and for a sufficient period of time to allow the antigen to bind to the dendritic cells (column 11, lines 51-57). Similarly, both Cohen et al. and Garbe et al. established appropriate culture conditions to induce the differentiation of monocytes, including those isolated from the blood of a patient having a cancer, into functional dendritic cells (Cohen et al., column 4, lines 13-18, column 5, lines 5-12 and lines 34-43; Garbe et al., see abstract). Patel discloses the making and using of flexible, autoclavable, plastic containers for storing red blood cells and these containers are able to suppress hemolysis of the red blood cells (See Summary of the Invention, columns 2 and 3) and have obvious properties as those recited in the claims.

Accordingly, at the time of the instant invention it would have been obvious to the ordinary skilled artisan to utilize functional dendritic cells derived from monocytes taught by Tedder et al., Cohen et al., Garbe et al. in the compositions taught by Edelson to arrive at the instant claimed invention. Furthermore, it would also have been obvious for one of ordinary skilled in the art to co-incubate the two cell populations in the disclosed compositions in an optimal period of time to allow the transfer of disease associated peptides from the treated disease effector cells to the MHC sites of the dendritic cells, and such compositions are contained in a blood collecting bag of the type taught by Patel. One of ordinary skilled in the art would have been motivated to

carry out the above modification because as taught by Edelson such compositions would improve or enhance immune responses to treat various diseases such as leukemia, lymphoma, autoimmune disease, graft versus host disease, and transplanted tissue rejection. Moreover, Edelson does not limit the use of dendritic cells derived from any particular source in his disclosed compositions (page 14, lines 26-30). Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Responses to Arguments

Applicants' arguments related to the above rejection in the Amendment filed on August 14, 2001 in Paper No. 9 (pages 12-13) have been fully considered.

Applicants mainly argued that "The Edelson (WO97/34472) reference does not add anything to the teachings of Garbe, Tedder, Edelson ('872 patent), Akagawa or Cohen regarding to the compositions set forth in claims 13-27 and 46-60". Particularly, the dendritic cells used in the method disclosed by Edelson (WO97/34472) are prepared using previously known dendritic cell culture methods separately from the photospheresis treatment of the blood. Furthermore, Applicants argued that "there is nothing in the Edelson (WO97/34472) reference that suggests that the method described in the Edelson '872 patent may be modified to produce functional antigen presenting dendritic cells by photospheresis". Examiner respectfully finds Applicants' arguments to be unpersuasive for the following reasons.

Firstly, it is noted that the instant claims are drawn to composition claims and not method claims. As such, the modified compositions resulting from the combined teachings of the Edelson (WO97/34472) in view of any one of Tedder, Garbe, Edelson ('872 patent), Akagawa or Cohen and in view of Patel (U.S. Patent No. 5,167,657) would possess the same properties as those of the instant claimed compositions for the reasons set forth above, and particularly for the reasons previously discussed with regard to the teachings of Tedder, Garbe, Edelson ('872 patent), Akagawa or Cohen.

Secondly, MPEP 2112.01 clearly states that "If the composition is physically the same, it must have the same properties". Additionally, MPEP 2112.02 clearly states that "While the references do not show a specific recognition of that result, its discovery by appellants (the induction of differentiation of monocytes into functional dendritic antigen presenting cells under photospheresis condition) is tantamount only finding a property in the old composition".

Accordingly, the claims remain rejected for the reasons set forth above.

Conclusions

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136 (a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed

within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortended statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136 (a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (703) 308-8339.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, Dave Nguyen, may be reached at (703) 305-2024, or SPE, Karen Hauda, at (703) 305-6608.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst, Patsy Zimmerman, whose telephone number is (703) 308-0196.

Quang Nguyen, Ph.D.

DAVE T. NGUYEN
PRIMARY EXAMINER